Research Report

Motor Cortex Organization After Stroke Is Related to Side of Stroke and Level of Recovery

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Background and Purpose—The present study hypothesized that side of stroke and level of recovery influence motor system organization after stroke.

Methods—Functional MRI was performed on 14 control subjects and 21 patients with chronic stroke during index finger tapping (control subjects, right; patients, recovered side).

Results—On functional MRI, stroke patients with right arm involvement showed (1) significantly smaller activation in contralateral motor cortexes compared with control subjects; (2) smaller ipsilateral (nonstroke) premotor and larger contralateral (stroke-side) sensorimotor activation compared with patients with left arm involvement, although electromyogram across groups was similar; and (3) 2.7-fold–larger contralateral sensorimotor cortex activation, ventrally, in those with full recovery compared with those with partial recovery, despite similar tapping force, frequency, range of motion, and electromyogram between groups. Supplementary motor area activation was unrelated to level of recovery.

Conclusions—After stroke that causes mild to moderate initial impairment and mild residual hand weakness, cortical organization varies with side of injury and with final motor status. The findings may have implications for treatment after stroke. **(*Stroke*. 2003;34:e23-e28.)**

Key Words: brain mapping ■ neuronal plasticity ■ recovery of function

Limited data are available relating level of final motor status after stroke to features of functional imaging brain activation maps. One goal of this study was to test the hypothesis that functional MRI (fMRI) motor activation maps vary in relation to final motor status.

Nondominant hand movements normally have different cortical organization than dominant hand movements, the former being more bilaterally organized in dextrals.[1,2] However, functional imaging studies have not examined whether motor system reorganization after stroke differs when nondominant compared with dominant hand is affected. When side of stroke influences poststroke physiotherapy, it is usually on the basis of associated cognitive symptoms, but theoretically, differences in motor reorganization related to stroke side might also be important. The present study addressed the hypothesis that nondominant hand movements are organized differently than dominant hand movements chronically after stroke.

Materials and Methods

Subject Selection and Evaluation

Twenty-five patients with stroke >10 weeks previously that was associated with arm sensorimotor deficits and 14 control subjects gave informed consent. There were no differences in age or sex. Patients and control subjects were all right handed (Edinburgh Inventory). fMRI head motion eliminated 4 patients. Language or attention deficits were uncommon (1 of 21) and were unrelated to fMRI performance. Review of acute stroke records showed mostly mild strokes; only 6 patients had complete hand function loss. Affected muscles improved by fMRI.

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Each subject spent <5 minutes practicing tapping just before fMRI, during which surface electromyograph (EMG) measured 5 right and 5 left arm muscles.

Image Acquisition

fMRI was acquired as described previously,[3] with 5 cycles of rest alternating with tapping. Control subjects tapped their right index fingers; patients tapped their stroke-affected side on top of a force transducer. Wrist splints restricted metacarpophalangeal flexion and extension to 25°. An in-room examiner verified tapping performances. Subjects tapped at 50% of the maximum rate (2-Hz limit).

Data Analysis

Data were analyzed as described previously.[3] Significantly ($Z>3$) activated voxels were counted in precentral gyrus, postcentral gyrus, supplementary motor area (SMA), premotor cortex, parietal operculum, frontal operculum, and remaining parietal lobe. Contralateral precentral gyrus signal change was measured (1% and 0.5% threshold). A >10% difference in pegboard performance (normal right-left

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Key Clinical and fMRI Results

Group	n	Time After Stroke, days	Stroke Volume, cm^3	Fugl-Meyer Score	Pegboard Score	Tap Rate, Hz	% Signal Change (1% Threshold)	Premotor Cortex Activation, voxels		
								Contralateral	Ipsilateral	Motor-Laterality Index
Control subjects	14	...	...	66	0.93	2.0	1.89	21	9	0.64
Left hand affected	10	136	68	62.0	0.67	1.5	1.73	11	21	0.17
Right hand affected										
Entire group	11	127	36	63.5	0.86	1.8	1.74	9	5	0.61
Full recovery	6	99	31	65.3	1.06	1.9	1.76	8	6	0.52
Partial recovery	5	157	38	61.4	0.62	1.7	1.71	10	3	0.71

Values are mean, except stroke volume and time after stroke (median). Pegboard score is number of pegs in Purdue Pegboard during separate 30-second trials for each hand, expressed as (affected hand)/(nonstroke hand); for controls, (left)/(right). Internal carotid artery narrowing (3/10 left-hand vs 3/11 right-hand involvement), deep stroke (2/10 vs 3/11), and prior stroke radiologically (3/10 vs 5/11) were evenly distributed among patient groups.

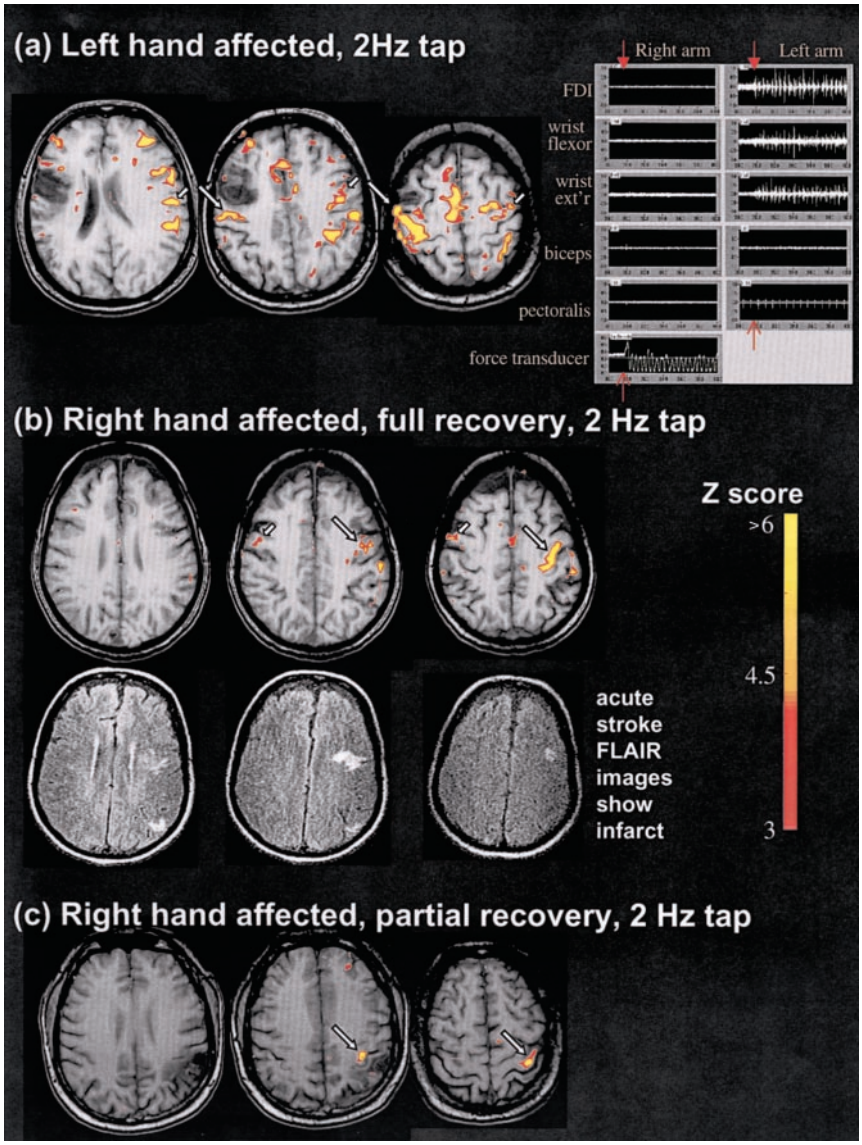

Figure 1. Individual patient activation maps. In a, bilateral brain activation was accompanied by unilateral EMG activity. Large arrows indicate contralateral (stroke-side) sensorimotor cortex activation; small arrows, ipsilateral (not stroke-side) motor-premotor cortex.

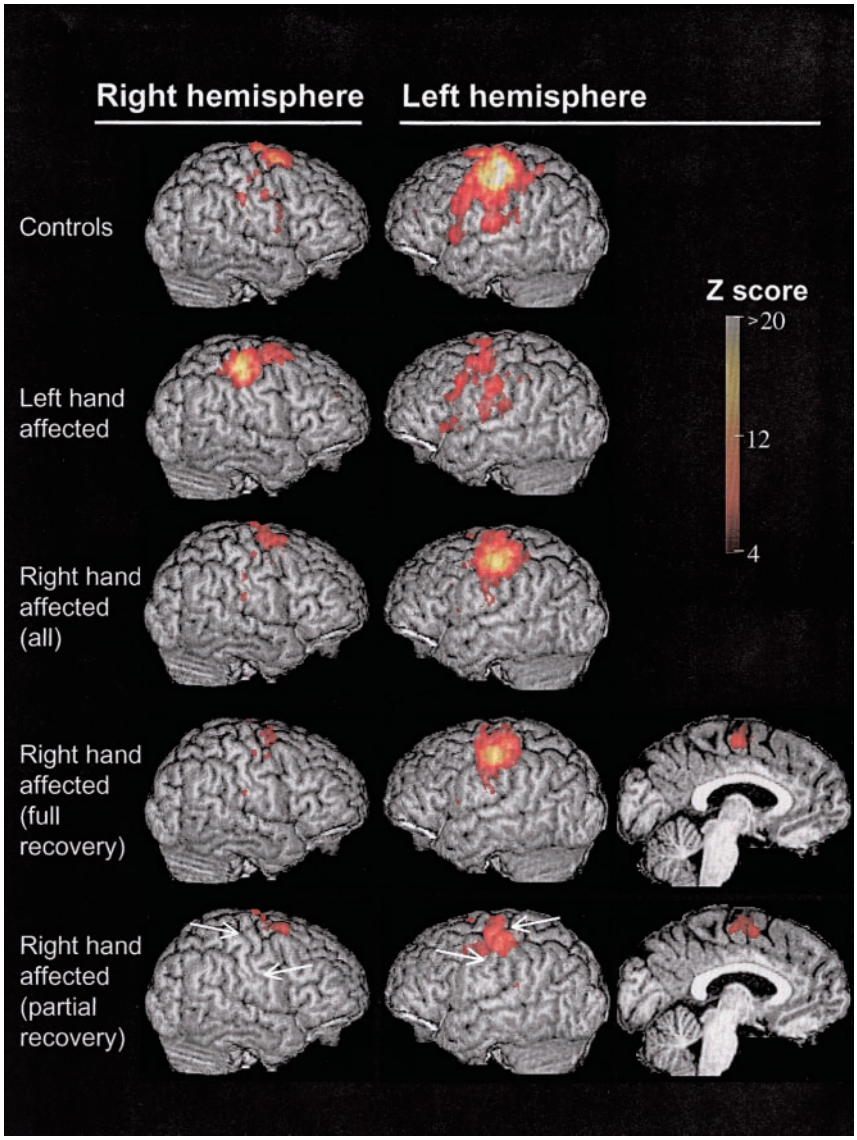

Figure 2. Group activation maps superimposed on normal brain anatomy. Arrows indicate central sulcus.

asymmetry) between affected and unaffected hands separated right-hand–affected patients into full or partial recovery. Group maps were generated in stereotaxic space and then contrasted pairwise by use of the 2-sample test statistic to reduce impact of different group sizes. Group and group contrast maps were then probed for significant ($Z>4$) activation clusters; Wilcoxon signed-rank test compared continuous measures. An all motor area–laterality index[2] was calculated.

Results

Effect of Stroke

No EMG leads showed significant differences between control subjects and right-arm–affected patients. Voxel counting found larger activation in control subjects within contralateral premotor cortex ($P<0.03$). When contrasting group maps, we found that control subjects showed significantly larger contralateral precentral gyrus and SMA activation.

Effect of Stroke Side

Patients who were right arm affected had no significant clinical differences compared with those who were left arm affected: smaller wrist extensor EMG on resting side (0% versus 19%, $P<0.01$), which was minute compared with active side (610% versus 498%, $P=$NS); smaller voxel counts within nonstroke (ipsilateral) premotor cortex ($P<0.05$, the Table and Figure 1); higher motor-laterality index (more contralateral, $P<0.05$); and when group maps were contrasted, significantly larger contralateral sensorimotor and smaller ipsilateral premotor plus SMA activation (Figure 2).

Effect of Recovery Level

Right-arm–affected patients with full recovery showed no clinical differences compared with those experiencing partial recovery, apart from pegboard results: in group maps, 2.7-fold–larger contralateral sensorimotor activation, with negligible differences in SMA; no differences in tapping force (1.03 versus 1.2 N, $P=$NS) or EMG; and when group maps were contrasted, a significant contralateral sensorimotor cortex focus ventrally at Talairach (30, −20, 45). Correlation analysis (SPM99), limited by the small sample size ($n=11$), did not find a linear relationship between activation and pegboard performance.

Reanalysis with threshold $Z=4$ (voxel counting) or $Z=3$ (cluster detection) minimally affected results. Contralateral percent signal change results did not differ between groups at either threshold and were not influenced by arterial disease. Negative activation maps showed no significant foci.

Discussion

Side of stroke and final motor status are related to motor system organization after stroke. Measurement of prescan EMG plus in-scan tapping force suggests that findings are related to changes in brain function rather than divergent movement performances.

Side of stroke influenced results, a finding relevant to occupational therapy. Greater ipsilateral premotor cortex recruitment is normally seen with left compared with right hand movement.[1] Such ipsilateral recruitment increases after stroke.[2,4–7] Ipsilateral recruitment varies according to stroke side (see Figures 1 and 2). Conclusions would be stronger if control left tapping data were available.

The best return of motor function after dominant-hemisphere stroke is related to preservation of function in affected hemisphere sensorimotor cortex, especially ventrally.[5] Results are consistent with transcranial magnetic stimulation studies,[8] which suggest that neurophysiological integrity of the affected hemisphere corticospinal tract is important to motor outcome. The basis for smaller activation with lesser recovery, despite movements similar to those of patients with full recovery, may relate to activity of subcortical areas not imaged.[9]

A previous functional imaging study found that stroke topography influences motor system reorganization.[10] Present results indicate that stroke side and final motor status are also important. Restorative therapy trials, as with acute and preventative trials, might reduce variance and increase power if patients are enrolled or stratified on the basis of clinical and physiological assessments relevant to recovery processes.

References

1. Kim S-G, Ashe J, Hendrich K, Ellermann JM, Merkle H, Ugurbil K, Georgopoulos AP. Functional magnetic resonance imaging of motor cortex: hemispheric asymmetry and handedness. *Science*. 1993;261: 615–617.
2. Cramer SC, Nelles G, Benson RR, Kaplan JD, Parker RA, Kwong KK, Kennedy DN, Finklestein SP, Rosen BR. A functional MRI study of subjects recovered from hemiparetic stroke. *Stroke*. 1997;28: 2518–2527.
3. Cramer SC, Mark A, Barquist K, Nhan H, Stegbauer KC, Price R, Bell K, Odderson IR, Esselman P, Maravilla KR. Motor cortex activation is preserved in patients with chronic hemiplegic stroke. *Ann Neurol*. 2002; 52:607–616.
4. Chollet F, DiPiero V, Wise RJS, Brooks DJ, Dolan RJ, Frackowiak RSJ. The functional anatomy of motor recovery after stroke in humans: a study with positron emission tomography. *Ann Neurol*. 1991;29:63–71.
5. Weiller C, Ramsay SC, Wise RJS, Friston KJ, Frackowiak RSJ. Individual patterns of functional reorganization in the human cerebral cortex after capsular infarction. *Ann Neurol*. 1993;33:181–189.
6. Seitz RJ, Hoflich P, Binkofski F, Tellmann L, Herzog H, Freund H-J. Role of the premotor cortex in recovery from middle cerebral artery infarction. *Arch Neurol*. 1998;55:1081–1088.
7. Calautti C, Leroy F, Guincestre JY, Baron JC. Dynamics of motor network overactivation after striatocapsular stroke: a longitudinal PET study using a fixed-performance paradigm. *Stroke*. 2001;32:2534–2542.
8. Binkofski F, Seitz RJ, Arnold S, Classen J, Benecke R, Freund HJ. Thalamic metabolism and corticospinal tract integrity determine motor recovery in stroke. *Ann Neurol*. 1996;39:460–470.
9. Belhaj-Saif A, Cheney PD. Plasticity in the distribution of the red nucleus output to forearm muscles after unilateral lesions of the pyramidal tract. *J Neurophysiol*. 2000;83:3147–3153.
10. Feydy A, Carlier R, Roby-Brami A, Bussel B, Cazalis F, Pierot L, Burnod Y, Maier MA. Longitudinal study of motor recovery after stroke: recruitment and focusing of brain activation. *Stroke*. 2002;33:1610–1617.